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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/876,252	06/07/2001	Dominic P. Behan	AREN-0240	8181

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BASI, NIRMAL SINGH

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/876,252	Applicant(s) Behan et al
	Examiner Nirmal S. Basi	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 23, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *101-132* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *101-132* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Response filed 01/23/03 (paper number 5) has been entered. Preliminary Amendment filed 6/7/01 (paper number 2) was entered in part. The amendment stating , "Please delete the Sequence Listing on file and renumber following pages accordingly" was not entered because there are two sets of sequence listings on file. Applicant should indicate which of the sequence listings should be deleted, i.e contained on pages 62-177 in the specification or pages 1-87 following the Abstract.

Election/Restriction

2. Applicant's election with traverse of Group XXVII, Claims 93, 95 and 96, in Paper No. 5 (1/23/03), is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement. Applicant has canceled claims 1-100, and added new claims 101-132. Claims 101-132, drawn to the elected invention of Group XXVIII will be examined.

3. ***Sequence Rules Compliance***

This application fails to comply with the sequence rules, 37 CFR 1.821-1.825. Nucleotide and polypeptide sequences must be identified with the corresponding SEQ ID NO. Title 37, Code of Federal Regulations, Section 1.821 states "reference must be made to the sequence by use of the assigned identifier", the identifier being SEQ ID NO. Sequences in Figure 1 must be identified by their corresponding SEQ ID NO:. Correction is required.

Specification

4. Acknowledgment is made of applicant's claim for priority. It is noted, however, that the priority information on page 2 of the specification, fails to disclose the U.S. Provisional Applicant numbers of many of the priority documents, as well as the relationship to co-pending U.S. Application AREN-0050 and 09,364,425. Applicant is required to provide all missing priority number information, the relationship of co-pending Application AREN-0050 and 09,364,425 to instant Application and the correct Application number of U.S. Application number of "AREN-0050".

Appropriate correction is required.

Further, according to the priority information, it appears that priority is being claimed to a large number of utility and provisional applications. These applications appear to be drawn to unrelated subject matter and are either not available for consideration or for which consideration to determine support for instantly claimed subject matter would require an undue burden. Accordingly, the subject matter defined in claims 101-132 has an effective filing date of June 7 2001 that of instant application. Applicants are requested to provide the serial number and specific page number(s) of any parent application to which priority is desired which specifically supports the particular limitation for each and every claim limitation in the pending claims which applicant considers to have been in possession and fully enabled of prior to 6/7/01.

Claim Rejection, 35 U.S.C. 112

5. Claims 102 -108-116, 119-132 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 102, 110 and 119 are indefinite because it is not clear when a polynucleotide is "consisting essentially" of the nucleotide sequence of SEQ ID NO:129 as compared to when it is not "consisting essentially" of the nucleotide sequence of SEQ ID NO:129 so as to allow the metes and bounds of the claim to be determined. Further, the claim is indefinite because it is not clear when a polynucleotide is "consisting essentially" of the nucleotide sequence consisting of a coding sequence for the polypeptide of SEQ ID NO:130 as compared to when it is not "consisting essentially"of the nucleotide sequence consisting of a coding sequence for the polypeptide of SEQ ID NO:130 so as to allow the metes and bounds of the claim to be determined. Also, the claim is indefinite because it is not clear when a polynucleotide is "consisting essentially" of the nucleotide sequence encoding the polypeptide of SEQ ID NO:130 as compared to when it is not "consisting essentially"of the nucleotide sequence encoding the polypeptide of SEQ ID NO:130 so as to allow the metes and bounds of the claim to be determined. "Consisting essentially of" does not give a quantitative measure of the length or composition of the claimed polynucleotide.

Claims 103-108, 11-116, 120-132 are indefinite because they depend on an indefinite base claim and fail to resolve the issues raised above.

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 101-132 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

A "specific utility" is a utility that is specific to the subject matter claimed, as opposed to a "general utility" that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention.

Applicant has asserted utilities for the specifically claimed invention of claims 101-132. The invention is directed to a polynucleotide, SEQ ID NO:129, encoding a non-endogenous, constitutively activated version of a human G protein coupled receptor comprising GPR38 (V279K), SEQ ID NO:130, vector comprising said polynucleotide, host cell comprising said plasmid and fusion constructs of said polynucleotide. The specification contains numerous polynucleotides encoding various G protein coupled receptors (GPCR). The specification gives generic uses to may of the GPCRs, suggested uses are: direct identification of candidate compounds as receptor agonists, inverse agonists or partial agonists having potential applicability as therapeutic agents, receptor screening, disease/disorder identification and/or selection, medicinal chemistry and in pharmaceutical compositions. The specification discloses general functional activities of G-protein coupled receptors (GPCR) which may be applicable to G-protein coupled receptors but does not disclose any activity associated with the specific GPR38 (V279K), of instant invention. Further no ligands that bind or activate GPR38 (V279K), are disclosed. The specification discloses that GPR38 (V279K), of the present invention may be a member of the GPCR protein family. In light of the specification the skilled artisan can only speculate that GPR38 (V279K), of instant invention is a protein belonging to the GPCR protein family. However, no disclosure is provided within the instant specification on what specific function a putative GPR38 (V279K), protein possesses, or ligands that bind, promoters that

activate; nor are any cell types/tissues disclosed that specifically express this protein; nor are any disease states disclosed that are directly related to GPR38 (V279K), dysfunction.

Mudroch et al (Review Article, see IDS) discloses, the superfamily of G-protein-coupled receptors are highly divergent in their effects and include receptors for hormones, neurotransmitters, paracrine substances, inflammatory mediators, certain proteinases, taste and odorant molecules, and even photons and calcium ions (page 3032, introduction). Members of a sub-family of G-protein-coupled receptors are also highly divergent in their effects, as highlighted by Mudroch et al, in the discussion of cytokine G-protein-coupled receptors (see pages 3032-3039). The utility of GPR38 (V279K), cannot be implicated solely from homology to known G-protein coupled receptors because the art does not provide teaching stating that all members of a sub-family of G-protein coupled receptors must have the same effects, the same ligands and be involved in the same disease states, the art discloses evidence to the contrary. For example, Mudroch et al discloses even though CCR6 is a member of the chemokine G-protein coupled receptors family and IL-2 was shown to up-regulate CCR6 mRNA recent data contradict this finding, and as a consequence, the effect of IL-2 on CCR6 expression remains uncertain (page 3035, second column, first paragraph). The GPR38 (V279K), of instant invention is considered by the examiner to be a member of the orphan receptor of G-protein coupled receptors i.e. seven transmembrane receptor with no known endogenous ligands. Watson et al (See IDS) devote a whole chapter to orphan G-protein coupled receptors and group them separately because even though the orphan receptors posses a certain degree of homology to G-

protein coupled receptors with known function, the orphan receptors require further research before they can be classified into one of the groupings of known G-protein coupled receptors (Watson et al, pages 223-230). Further, a position that the GPR38 (V279K), is related, through homology, to known orphan receptors may be true, but the art shows it requires more than the disclosed homology to assign a function to an orphan receptor, knowledge of the endogenous ligand for the receptor is required. The assumption that an orphan receptor be placed in a particular group is not always true as highlighted by the statement Watson, who states, "It was originally claimed that the human homologue of RDC1 codes for VIP receptor, but this is no longer thought to be correct" (page 228).

The specification discloses general functional activities of GPCRs which may be applicable to claimed GPR38 (V279K), but does not disclose any activity associated with the specific GPR38 (V279K), or related GPR38 (V279K). Also, ligands that bind GPR38 (V279K), may not interact, with the natural GPR38 (V279K),, in the same manner or even have the same effect. Further no ligands that bind or activate GPR38 (V279K), or related GPR38 are disclosed.

The utilities asserted by Applicant are not specific or substantial. Since no specific function of the polypeptide of instant invention is known, and the hypothesized function is based entirely on conjecture from homologous polypeptides, the asserted utilities are not specific to instant polypeptide, but rather are based on family attributes. Neither the specification nor the art of record disclose the GPR38 (V279K), fragments or variants thereof useful to identify drugs that affect said protein and modulate its activity. Similarly, neither the specification nor the art

of record disclose any instances where disorders can be effected by interfering with the activity using the GPR38 (V279K), or related GPR38, or using fragments or variants thereof. Thus the corresponding asserted utilities are essentially methods of using GPR38 (V279K), to identify disease states associated with GPR38 (V279K), disfunction and as targets for drug discovery. Therefore the asserted utilities are essentially methods of testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating or testing for compounds that interact with GPR38 (V279K), which may be implicated in an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed GPR38 (V279K),, further experimentation is necessary to attribute a utility to the claimed polypeptides and fragments thereof. See Brenner v. Manson, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed GPR38 (V279K), further experimentation is necessary to attribute a utility to the claimed GPR38 (V279K),. The instant

application does not disclose the biological role of GPR38 (V279K), or its significance. The utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the GPR38 (V279K), of the instant invention. The disclosed protein, whose cDNA has been isolated, is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, a specific and substantial credible utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to

> be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

Claims 101-132 are drawn to a polynucleotide encoding a polypeptide with, as yet, undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the GPR38 (V279K), as of the filing date, useful for "diagnosis, prevention, and treatment of disease", such as cancers etc. Until some actual and specific significance can be attributed to the protein identified in the specification as GPR38 (V279K), , one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

The cDNA of the instant invention and the protein encoded thereby are compounds which share some structural similarity to receptor proteins having GPCR domains based on sequence similarity. As disclosed by the specification, the family of proteins related to GPR38 (V279K), may have diverse effects and bind a diverse number of ligands. The family of proteins having GPCR like domains have different levels of expression, and play roles in the pathogenesis of various diseases. Although the family of receptor proteins having GPCR like domains may share some common structural motifs, various members of the family may have different sites of action and different biological effects. In the absence of knowledge of the ligand for GPR38 (V279K), or the biological significance of these proteins, there is no immediately evident patentable use. To employ a protein of the instant invention in any of the disclosed methods

would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for GPR38 (V279K),, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

Neither the specification nor the art of record disclose GPR38 (V279K), or fragments thereof useful to identify drugs that affect said protein and modulate its activity. Similarly, neither the specification nor the art of record disclose any instances where disorders can be effected by interfering with the activity using the GPR38 (V279K) . Thus the corresponding asserted utilities are essentially methods of using GPR38 (V279K), to identify disease states associated with GPR38 (V279K), disfunction and as targets for drug discovery. Therefore the asserted utilities are essentially methods of testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating or testing for compounds that interact with GPR38 (V279K), which may be implicated in an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed GPR38 (V279K), , further experimentation is necessary to attribute a utility to the claimed GPR38 (V279K), . Further since the nucleic acid encoding GPR38 (V279K), receptor or the encoded polypeptide are not supported by either a specific and substantial asserted utility or a well established utility, it follows that the methods of

using GPR38 (V279K), are also not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above

Further, with regard to diagnosis of disease, in order for a polypeptide or protein to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polypeptide and a disease or disorder. The presence of a polynucleotide in tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed cDNA or protein and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polypeptide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. over expression). Evidence of a differential expression might serve as a basis for use of the claimed polypeptide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the polynucleotide or the claimed polypeptide that is encoded thereby and any disease or disorder and the lack of any correlation between the polynucleotide or the encoded claimed polypeptide with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no

patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

Further, the rejection is based on the failure to disclose sufficient properties of the protein and/or polynucleotide to support an inference of utility. GPR38 (V279K), belongs is a family in which the members have divergent functions. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family.

The diversity of the biochemical function and the wide range of regulatory pathways involving GTP-binding proteins is well known in the art. Without some common biological activity for the family members, a new member would not have a specific, substantial, or credible utility when relying only on the fact that it has structural similarity to the other family members. The members of the family have different biological activities which may be related to tissue distribution but there is no evidence that the claimed compounds share any one of diverse number of activities. That is, no activity is known to be common to all members. To argue that all the members can be used for toxicology testing, diagnosis is to argue a general, nonspecific

utility that would apply to virtually every member of the family, contrary to the evidence. Further, any compound could be considered as a regulator or modulator of tissue in that any compound, if administered in the proper amount, will stimulate or inhibit tissue. For example, salt, ethanol, and water are all compounds which will kill cells if administered in a great enough amount, and which would stimulate cells from which these compounds had been withheld, therefore, they could be considered regulators or modulators of tissue. However, use of these compounds for the modulation of tissue would not be considered a specific and substantial utility unless there was some disclosure of, for example, a specific and particular combination of compound/composition and application of such in some particular environment of use. Further, the specification does not disclose the significance of any test results, nor is there any evidence that the significance was known as of the filing date. If the expression of the claimed GPR38 (V279K), increases, is this a positive or negative outcome? Would this be a toxic response or not? The disclosure is insufficient to evaluate the results of the test in any meaningful manner.

Without knowing a biological significance of the claimed polypeptides, one of ordinary skill in the art would not know how to use the claimed invention in its currently available form in a credible "real world" manner based on the diversity of biological activities possessed by GTP-binding proteins. Contrast *Brenner*, 148 USPQ at 694 (despite similarity with adjacent homologue, there was insufficient likelihood that the steroid would have similar tumor-inhibiting characteristics), with *In re Folkers*, 145 USPQ 390, 393 (CCPA 1965) (some uses can be immediately inferred from a recital of certain properties) or *In re Brana*, 34 USPQ 1436, 1441

(Fed. Cir. 1995) (evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility; here, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement).

The implication that the claimed invention has utility in toxicology testing, drug development and disease diagnosis, do not meet the standards for a specific, substantial, and credible or well-established utility for reasons set forth above.

Further, Applicant infers that a utility may be specified even if it applies to a broad class of inventions. The proposition is not sufficient to establish utility for each member of the class. Specific utility must be shown or be evident for each member of the class. None of the utilities identified by Applicant, i.e. toxicology testing, drug discovery, disease diagnosis, have been demonstrated to be specific to the compounds of GPR38 (V279K), . One of ordinary skill in the art must understand how to achieve an immediate and practical benefit from the claimed species based on the knowledge of the class. However, no practical benefit has been shown for the use of GPR38 (V279K), .

In all cases a practical utility of an invention may be derived from belonging to a broad class of inventions. The requirement in any particular case, however, is that practical utility can be inferred if each and every member of the broad class possesses a common utility. The question in the instant application is whether the members of the family of proteins to which the claimed invention is structurally related have, individually, a specific, substantial and credible or well-established utility. Applicant has failed to show by a preponderance of the evidence, in

enough detail, with respect to the described GPR38 (V279K), has any substantial use. The record shows that the GTP-binding protein family is diverse, and has such a broad definition, that a "common utility" cannot be defined. Moreover, the evidence of record is inadequate to determine the disease(s), drug(s) or toxicological screen(s) for which the compounds would be useful. In *Brenner,* the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for possible tumor-inhibiting effects and an adjacent homologue of the compound had proven effective. *Brenner*, 148 USPQ at 690. Here, there is no evidence that the claimed isolated compounds have any utility.

7. Claims 101-132 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed cDNA encoding GPR38 (V279K), further experimentation is necessary to attribute a utility to the claimed polypeptides and fragments thereof.

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. a review of *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) clearly points out the factors to be considered in determining whether a disclosure would require undue experimentation and include (1) the quantity of experimentation necessary, (2) the amount of

direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors are considerations when determining the whether undue experimentation would be required to use the claimed invention. As is evidence in the discussions *supra*, each of these factors has been carefully considered in the instant grounds of rejection, and it is maintained that undue experimentation would be required by the skilled artisan to use the instant invention.

The specification implies that the use of the claimed invention for toxicology testing, drug discovery, and disease diagnosis are substantial utilities. The question at issue is whether or not the broad general assertion that the claimed nucleic acids might be used for *some* diagnostic application in the absence of a disclosure of *which* diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.')

1. The specification implies that since instant invention has some sequence homology to known orphan receptors that a reasonable correlation has been established and the asserted utility must be accepted. However, for reasons set forth above, the specification or prior art has not presented sufficient evidence to support specific utility for GPR38 (V279K),. The present rejection under § 101 follows *Brenner v. Manson*, as set forth above. In that case, the absence of a demonstrated specific utility for the claimed steroid compound was not ameliorated by the existence of a demonstrated general utility for the class. Unlike *Fujikawa v. Wattanasin*, where there were pharmaceutically acceptable in vitro results, here, there is nothing other than relatively low levels of sequence homology to a broad and diverse family of proteins having distinct modes of activity, and no disclosed common mode of action. As Applicant recognizes, a rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 20 00); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

RM 9. The IDS will be considered in the next office Action, they were not available at the time of writing this action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
March 24, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600